How to Write an NIH Proposal

Sally Bond
Assistant Director of Research Development Services
Proposal Coordination
Office of the Executive Vice President for Research and Partnerships
Purdue Research Development Services
Office of the Executive Vice President for Research and Partnerships

Funding and Grant Writing

The goal of the EVPRP Research Development staff is to assist faculty in the development of research and education proposals. EVPRP staff provide a broad range of services and resources related to funding and grantmanship. Below are some of the ways we can assist.

Funding Resources
The funding page provides information on internal, external, seed, and early investigator funding opportunities. Links to helpful funding search tools and email alerts can also be found here.

Limited Submissions
Check here for details on internal competitions including deadlines, templates and submission guidelines.

Grant Writing Services and Resources
Research Development staff can provide assistance with both large and small proposals. This page explains our services and provides links to other useful proposal preparation resources.

Site Visits
Our staff can assist with the logistics and coordination of site visits allowing the research team to focus on their science and team. Follow this link to find out more about these services.

Events
The events page provides information on upcoming grantmanship workshops and events including dates, times, and registration information. Presentations from previous events can also be accessed from this site.

Other Useful Links
Our Guide to the Grants Process at Purdue University and information on potential education and outreach partners are available here as well as links to other grantsmanship resources.

Questions, Comments, And Suggestions
We’d like to hear from you about services and resources that are valuable to you. Please e-mail us with questions, comments, and suggestions.
Where Do I Go for Help?

Hyperlinked “help” flowchart

A Visual Guide to the Grants Process at Purdue

Purdue Proposal Development Process

IDEA

Have funding opportunity? YES

Is funding limited? YES

Email Sue Grimes: EYPRlimited@purdue.edu

NO

Review funding options

Contact Pre-Award Center to begin budget development with a proposal specialist

LARGE

LARGE or consult level? YES

Went grant writing assistance? NO

Review self-help tools

CONSULT

Email Proposal Coordinator: proposalcoordinator@purdue.edu

Submits final proposal using institutional authority at Pre-Award Center
What Should Your Timeline Be?

Two months planning...two months writing

NIH Planning Timeline

NIH Writing Timeline
Reviewers Want to Know

Specific aims page is key. Reviewers ask themselves three questions....

- Are you solving something that is critical to solve?
- Are you solving it the right way?
- Are you the right person to do this work?
Planning Your Application

Do your homework...NIH e-reporter

• Find out what NIH institutions support research on your topic
• Assess funded projects
• Determine appropriate funding mechanisms

http://grants.nih.gov/grants/funding/funding_program.htm
Planning Your Application

Know the application process

Planning Your Application

Read the RFA or PA carefully for special instructions and review criteria

<table>
<thead>
<tr>
<th>Funding Opportunity Title</th>
<th>BD2K Support for Meetings of Data Science Related Organizations (U13)</th>
</tr>
</thead>
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<tr>
<td>Activity Code</td>
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<td>Catalog of Federal Domestic Assistance (CFDA) Number(s)</td>
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<td>Funding Opportunity Purpose</td>
<td>The purpose of this Funding Opportunity Announcement (FOA) is to support high quality and impactful conferences/ scientific meetings that are convened by data science related organizations whose missions focus on biomedical data science. This FOA, which uses the NIH-conference cooperative agreement program (U13), is part of the NIH-wide initiative Big Data to Knowledge (BD2K). Data science related organizations have a critical role in advancing biomedical data science but often depend on meetings to carry out their work. This FOA will support high quality conferences or meetings that are relevant to the biomedical data science needs of the participating Institutes and Centers of the National Institutes of Health. For the purpose of this FOA, a conference is defined as a gathering, as such as in the form of a symposium, seminar, scientific meeting, workshop, or any other organized and formal meeting where persons assemble to coordinate, exchange, and disseminate information, or to explore or clarify a defined subject, problem, or area of knowledge. Applicants representing data science related organizations may request support for one or a series of meetings over multiple years that address areas of data science aligned with the goals of the NIH BD2K program.</td>
</tr>
<tr>
<td>Key Dates</td>
<td></td>
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<tr>
<td>Posted Date</td>
<td>October 7, 2010</td>
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<tr>
<td>Open Date (Earliest Submission Date)</td>
<td>November 15, 2010</td>
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<tr>
<td>Letter of Intent Due Date(s)</td>
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<tr>
<td>Application Due Date(s)</td>
<td>December 15, 2018; November 31, 2018, by 5:00 PM local time of applicant organization. All types of applications allowed for this funding opportunity announcement are due on these dates. Applicants are encouraged to apply early to allow adequate time to make any corrections to errors found in the application during the submission process by the due date.</td>
</tr>
</tbody>
</table>
Prepare to Write: Focus on the Big Picture

Develop a compelling storyline

• What is the problem?
• What has been done already to address the problem?
• What is the gap that remains?
• How do you propose to address this gap?
Build the Storyline

Logic flow goes from broad to narrower

• What is the problem?
• What has been done already to address the problem?
• What is the gap that remains?
• How do you propose to address this gap?
Build the Storyline

What does this look like in NIH submission? Specific aims page template

Example of NIH-Style Outline

**Specific Aims Page (1 page limit)**

- State what is the human health problem. **Write** a compelling first sentence.
- Summarize what has been done already to address this problem.
- Clearly articulate the gap that still exists.
- State how you propose to address this gap:
  - Can have overarching hypothesis at this point and put the word **hypothesis** in bold italics.
  - May be appropriate to: state technologies you plan to use, describe expertise to do a task, map past accomplishments to your proposed work, explain the biology further, state how your aims work together.
  - State how this work is innovative.

**Aim 1:** List your concrete objective here in bold run-on header starting with strong verbs such as **identify, quantify, establish, determine.**

- Describe each aim in one to three sentences.
- Can have working hypothesis if needed (Aim must test hypothesis)
- Can tie to preliminary data
- Convey the "why" this work needs to be done as well as the "what" will be done.

**Aim 2:** List your concrete objective here in bold run-on header starting with strong verbs such as **identify, quantify, establish, determine.**

- Describe each aim in one to three sentences.
- Can have working hypothesis if needed (Aim must test hypothesis)
- Can tie to preliminary data
- Convey the "why" this work needs to be done as well as the "what" will be done.

**Aim 3:** List your concrete objective here in bold run-on header starting with strong verbs such as **identify, quantify, establish, determine.**

- Describe each aim in one to three sentences.
- Can have working hypothesis if needed (Aim must test hypothesis)
- Can tie to preliminary data
- Convey the "why" this work needs to be done as well as the "what" will be done.

- End with final paragraph on the expected outcomes of the research. What will you deliver/enable when you are successful? Should be at least one outcome per specific aim but also a general outcome.
Build the Storyline

Specific aims page is critical. You must make a good first impression.

- State what is the human health problem. Write a compelling first sentence.
- Summarize what has been done already to address this problem.
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NIAID Resources

Checklists, newsletter, and annotated grants

https://www.niaid.nih.gov/grants-contracts/apply-grant
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Build the Storyline

Example storyline starts your specific aims page

What is the problem?
What has been done already to address this problem?
What is the gap that remains?
How do you propose to address this gap?

Specific Aims

Microscopy has emerged as one of the most powerful and informative ways to analyze cell-based high throughput screening (HTS) samples in experiments designed to uncover novel drugs and drug targets. However, many diseases and biological pathways can be better studied in whole animals—particularly diseases that involve organ systems and multicellular interactions, such as metabolism and infection. The worm Caenorhabditis elegans is a well-established and effective model organism that can be robotically prepared and imaged, but existing image-analysis methods are insufficient for most assays. We propose to develop algorithms for the analysis of high-throughput C. elegans images, validating them in three specific experiments to identify chemicals to cure human infections and genetic regulators of host response to pathogens and fat metabolism. Novel computational tools for automated image analysis of C. elegans assays will make whole animal screening possible for a variety of biological questions not approachable by cell-based assays. Building on our expertise in developing image processing and machine learning algorithms for high-throughput screening, and on our established collaborations with leaders in C. elegans research, we will:

Carolina Wählby of the Broad Institute
Aim 1: List your concrete objective here in bold run-on header starting with a strong verb. Describe each aim in one to three sentences.

- Can have working hypothesis if needed
- Can tie to preliminary data
- Convey the “why” this work needs to be done as well as the “what” will be done
Writing Your Aims

Strong vs weak specific aim verbs

**Weak**: Investigate, study, correlate, describe

**Strong**: identify, determine, define, establish, quantify

Weak tends to not have a definitive end point.
Writing Your Aims

What you will accomplish, your approach, and impact

Specific Aims

Microscopy has emerged as one of the most powerful and informative ways to analyze cell-based high throughput screening (HTS) samples in experiments designed to uncover novel drugs and drug targets. However, many diseases and biological pathways can be better studied in whole animals—particularly diseases that involve organ systems and multicellular interactions, such as metabolism and infection. The worm Caenorhabditis elegans is a well-established and effective model organism that can be robotically prepared and imaged, but existing image-analysis methods are insufficient for most assays. We propose to develop algorithms for the analysis of high-throughput C. elegans images, validating them in three specific experiments to identify chemicals to cure human infections and genetic regulators of host response to pathogens and fat metabolism. Novel computational tools for automated image analysis of C. elegans assays will make whole animal screening possible for a variety of biological questions not approachable by cell-based assays. Building on our expertise in developing image processing and machine learning algorithms for high-throughput screening, and on our established collaborations with leaders in C. elegans research, we will:

Aim 1: Develop algorithms for C. elegans viability assays to identify modulators of pathogen infection

Challenge: To identify individual worms in thousands of two-dimensional brightfield images of worm populations infected by Microsporidia, and measure viability based on worm body shape (live worms are curvy whereas dead worms are straight).

Approach: We will develop algorithms that use a probabilistic shape model of C. elegans learned from examples, enabling segmentation and body shape measurements even when worms touch or cross.

Impact: These algorithms will quantify a wide range of phenotypic descriptors detectable in individual worms, including body morphology as well as subtle variations in reporter signal levels.
Carolina Wählby’s paragraph after her three specific aims:

In addition to discovering novel anti-infectives and genes involved in metabolism and pathogen resistance, this work will provide the C. elegans community with (a)......, (b)...., and (c)....
Specific Aims Page is the Master Plan

Provides a map of the rest of your proposal

• Significance
• Innovation
• Approach
Specific Aims Page is the Master Plan

Provides a map of the rest of your proposal

- Significance
- Innovation
- Approach
**Specific Aims**

Microscopy has emerged as one of the most powerful and informative ways to analyze cell-based high throughput screening (HTS) samples in experiments designed to uncover novel drugs and drug targets. However, many diseases and biological pathways can be better studied in whole animals—particularly diseases that involve organ systems and multicellular interactions, such as metabolism and infection. The worm Caenorhabditis elegans is a well-established and effective model organism that can be robotically prepared and imaged, but existing image-analysis methods are insufficient for most assays. We propose to develop algorithms for the analysis of high-throughput C. elegans images, validating them in three specific experiments to identify chemicals to cure human infections and genetic regulators of host response to pathogens and fat metabolism. Novel computational tools for automated image analysis of C. elegans assays will make whole animal screening possible for a variety of biological questions not approachable by cell-based assays. Building on our expertise in developing image processing and machine learning algorithms for high-throughput screening, and on our established collaborations with leaders in C. elegans research, we will

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**Research Strategy**

**A Significance**

The NIH is committed to translating basic biomedical research into clinical practice and thereby impacting global human health, and Francis Collins identifies high-throughput technology as one of five areas of focus for the NIH’s research agenda. For many diseases, researchers have identified successful novel therapeutics or research probes by applying technical advances in automation to high-throughput screening (HTS) using either biochemical or cell-based assays. Researchers are using genetic perturbations such as RNA interference or gene overexpression in cell-based HTS assays to identify genetic regulators of disease processes as potential drug targets. However, the molecular mechanisms of many diseases that deeply impact human health worldwide are not well-understood, and thus cannot yet be reduced to biochemical or cell-based assays.

Ideally, researchers could approach disease from a phenotypic direction, in addition to the traditional molecular approach, by searching for chemical or genetic regulators of disease processes in whole model organisms rather than isolated cells or proteins. Moving HTS towards more intact, physiological systems also improves the likelihood that the findings from such experiments accurately translate into the context of the human body (e.g., in terms of toxicity and bioavailability), simplifying the path to clinical trials and reducing the failure of potential therapeutics at later stages of testing. In fact, for some diseases, a whole organism screen may actually be necessary to break new therapeutic ground, in the search for novel therapeutics for infectious agents, for example, it is widely speculated that the traditional approach of screening for chemicals that directly kill bacteria in vitro has been largely exhausted. Our work recently identified novel classes of chemicals that cure model organisms of infection by the important human pathogen E. faecalis through mechanisms distinct from directly killing the bacterium itself. Antimicrobials with new mechanisms of action are urgently needed to combat widespread antibiotic resistance in pathogens.

Enabling HTS in whole organisms is therefore recognized as a high priority (NIH P01-08-024). C. elegans is a natural choice. Manually-analyzed RNAi and chemical screens are well-proven in this organism, with dozens completed. Many existing assays can be adapted to HTS, instrumentation exists to handle and culture C. elegans in HTS-compatible multi-well plate organ systems have high physiologic similarity and genetic conservation with humans. C. elegans is particularly suited to assays involving visual phenotypes: physiologic abnormalities and fluorescent markers are easily observed because the worm is mostly transparent. The worms follow a stereotypic developmental pattern that yields identically-appearing adult adults, such that deviations from wild-type are more readily apparent.

The bottleneck that remains for tackling important human health problems using C. elegans HTS is image analysis (NIH PA-07-320). It has been recently stated, “Currently, one of the biggest technical limitations for large-scale RNAi-based screens in C. elegans is the lack of efficient high-throughput methods to quantitate lethality, growth rates, and other morphological phenotypes.” Our proposal to develop image analysis algorithms to identify regulators of infection and metabolism in high-throughput C. elegans assays would bring image-based HTS to whole organisms, and have the following impact:

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Specific Aims Page is the Master Plan

Provides a map of the rest of your proposal

• Significance
• Innovation
• Approach

STORYLINE INTRO
CLOSING PARAGRAPH
Innovation and Impact

Summarize long-term impact at end of specific aims page

Carolina Wähly's paragraph after specific aims:

Aim 3: Develop algorithms for gene expression pattern assays to identify regulators of the response of the C. elegans host to Staphylococcus aureus infection
Challenge: To map each worm to a reference and quantify changes in fluorescence localization patterns.
Approach: We will develop worm mapping algorithms and combine them with anatomical maps to extract atlas based measurements of staining patterns and localization. We will then use machine learning to distinguish morphological phenotypes of interest based on the extracted features.
Impact: These algorithms will enable addressing a variety of biological questions by measuring complex morphologies within individual worms.

In addition to discovering novel anti-infectives and genes involved in metabolism and pathogen resistance, this work will provide the C. elegans community with (a) a versatile, modular, open-source toolbox of algorithms readily usable by biologists to quantify a wide range of important high-throughput whole-organism assays, (b) a new framework for extracting morphological features from C. elegans populations for quantitative analysis of this organism, and (c) the capability to discover disease-related pathways, chemical probes, and drug targets in high-throughput screens relevant to a variety of diseases.

Primary collaborators
Specific Aims Page is the Master Plan

Provides a map of the rest of your proposal

- Significance
- Innovation
- Approach

STORYLINE INTRO
CLOSING PARAGRAPH
AIMS
Aim 1: Develop algorithms for C. elegans viability assays to identify modulators of pathogen infection. 

Challenge: To identify individual worms in thousands of two-dimensional brightfield images of worm populations infected by Microsporidia, and measure viability based on worm body shape (live worms are curvy whereas dead worms are straight).

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Impact: These algorithms will quantify a wide range of phenotypic descriptors detectable in individual worms, including body morphology as well as subtle variations in reporter signal levels.
Significance

Your research must solve a critical problem

• Write for broad scientific audience
• Answer the “so what?” not the “how.” If your research works as proposed, will your results be important for the field?
• Address the gap as a natural extension of your research
Innovation

Not status quo but enabling a new direction to the research area

- Innovation can be in your new theory or in your novel methods and tools
- Fresh point of view or new technology
Approach

Describes your experimental design

• Is your project workable as described?
• When you are done, will the results be clear?
• Relate each specific aim back to your storyline and show how results will help address gap
• Include quality tables and figures with clear labels accurate with text
Preliminary Data

Purpose is extension and feasibility

- naturally extends your existing research but not merely incremental advances
- assures reviewers that what you propose will be feasible
- be clear which data are yours and which are other teams
Two Options for Preliminary Data

Outline to be consistent in format for a well-structured approach section

Title of Specific Aim #1

Introduction to Approach

Justification and Feasibility

Review of relevant literature

Preliminary studies

Research Design

Expected Outcomes

Potential Problems and Alternative Strategies
Two Options for Preliminary Data

Outline to be consistent in format for a well-structured approach section

Preliminary Studies (for all the aims together)
Title of Specific Aim #1 (verbatim from your specific aims section)
  – Introductory paragraph

Research Design

Expected Outcomes

Potential Problems and Alternative Strategies
Rigor and Reproducibility

How scientifically sound and replicable are the studies?


FAQs
http://grants.nih.gov/reproducibility/faqs.htm#II
Internal Review

We can help find experienced reviewers to provide feedback

NIH Writing Timeline
Questions?
Writing a Proposal to NIH

Perry Kirkham
National Institutes of Health
Grants Process
At-A-Glance

Planning, Writing, and Submitting

Planning: Applicant should start early, collect preliminary data, and determine internal deadlines.

Writing: Applicant often begins writing application several months prior to application due date.

Submitting: Applicant organization submits most applications to NIH through the Federal portal, Grants.gov.

Receipt and Referral

1 – 3 Months

Applications compliant with NIH policies are assigned for review by the Division of Receipt and Referral in the Center for Scientific Review (CSR).

CSR assigns application to an NIH Institute/Center (IC) and a Scientific Review Group (SRG).

Scientific Review Officer (SRO) assigns applications to reviewers and readers.

Peer Review

4 – 8 Months

Initial Level of Review: SRG members review and evaluate applications for scientific merit.

Priority Scores: Available to Principal Investigator in eRA Commons.

Summary Statement: Available to Principal Investigator in eRA Commons.

Second Level of Review: Advisory council/board reviews applications.

Award

9 – 10 Months

Pre-Award Process: IC grants management staff conducts final administrative review and negotiates award.*

Notification of Award: Institute/Center issues and sends Notice of Award (NoA) to applicant institution/organization.

Congratulations! Project period officially begins!

Post-Award Management

Administrative and fiscal monitoring, reporting, and compliance

Visit: http://grants.nih.gov/grants/grants_process.htm for more about the NIH grants process
Twofold Mission:

1. Assign proposals

Receipt and referral –

a. read as much of the proposal as necessary to make an appropriate assignment (suitability, IC, dual assignment, review)

b. consider the PI request
Twofold Mission:

2. achieve optimal peer review

Peer Review – IRG (study section)

http://cms.csr.nih.gov/PeerReviewMeetings/CSRIRGDescriptionNew/

CB – Cell Biology (IRG)

  BDPE – biology and diseases of the posterior eye (SS)
  NCSD – nuclear and cytoplasmic structure/function and dynamics (SS)
  CMAD – cellular mechanisms in aging and development (SS)
  CSRS – cellular signaling and regulatory systems (SS)
  DEV1 – development 1 (SS)
  DEV2 – development 2 (SS)
The Center for Scientific Review (CSR) is the portal for NIH grant applications and their review for scientific merit. We receive all research grant applications sent to NIH and handle the review of more than 70% of those by organizing peer review groups (study sections) to evaluate research grant applications. Our mission is to see that NIH grant applications receive fair, independent, expert, and timely reviews – free from inappropriate influences – so NIH can fund the most promising research.

Find a Study Section

Applications are reviewed in Study Sections (Scientific Review Group, SRG). Integrated Review Groups (IRGs) are clusters of Study Sections based on scientific discipline.

Search Integrated Review Group (IRG) / Study Group
Study Section

BDPE

http://cms.csr.nih.gov/PeerReviewMeetings/CSIRGDescriptionNew/CBIRG/BDPE.htm

Topics covered
Membership roster (standing members) **
Meeting roster (reviewers for a specific meeting)
SRA (SRO)
Study sections with areas of similar science
**What are they looking for?**

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**Project Information**

<table>
<thead>
<tr>
<th>DESCRIPTION</th>
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<tbody>
<tr>
<td>Project Number:</td>
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<tr>
<td>Title:</td>
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</table>

**Contact PI Information:**

Name: ALEXANDER, CAROLINE MARGARET
Email: alexander@oncology.wisc.edu
Title: ASSOCIATE PROFESSOR

**Program Official Information:**

Name: SATYAMOORTHY, NEERAJA
Email: nso@nih.gov

**Organization:**

Name: UNIVERSITY OF WISCONSIN MADISON
City: MADISON
Country: UNITED STATES (US)

**Other Information:**

RAAIPA: PA-07-079
Study Section: Molecular Oncogenesis Study Section (MONO)
Fiscal Year: 2011
Award Notice Date: 20-DEC-2010

**Administering Institutes of Centers:**

NATIONAL CANCER INSTITUTE

**Project Funding Information for 2011:**

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<th>Year</th>
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</table>
What are they looking for?
“It was generally seen that integrating preliminary data with the appropriate aim was an effective approach. Both too little preliminary data and too much preliminary data were seen as ineffective. "Shortchanging" preliminary data hurt scores, particularly if the data were relevant to the innovation. Even with published data, including enough context is key. The proposal should be able to stand on its own, and the burden is on the applicant to make certain that there is enough information for the reviewers.”

“The most consistently effective strategy for the Approach was to treat each aim like a story. These proposals integrated necessary background information and preliminary data into the approach for each aim.: 

“Some investigators chose to "save space" by not using any figures. This was considered a major failing. Lack of figures or tables and lack of white space indicated that the grant writer was having difficulty adapting to the new format, and this approach was not viewed favorably.”
Summary Statement

Who is the program officer?
What are the salient points?
Who made the salient points?
Which of those can you address easily?
Which must you address?
What was discussed

What is not in the text?

What is the “tenor” of the discussion
Response to Scientific Review

What next?

Go forward with a revision?
Go forward with a new application?
Revise but request a different study section?
Write a new application using the same study section?
SUMMARY STATEMENT

Application Number: 1 R01 GM095672-01

PROGRAM CONTACT:
JOSEPH GINDHART JR
301-594-0828
gindhartjg@mail.nih.gov

Principal Investigator
WAHLBY, CAROLINA EWA ASA PHD

Applicant Organization: BROAD INSTITUTE, INC.

Review Group: MI
Microscopic Imaging Study Section

Meeting Date: 06/03/2010
Council: OCT 2010
Requested Start: 12/01/2010

RFA/PA: PA10-067
PCC: C104GJ

Project Title: Image analysis for high-throughput C. elegans infection and metabolism assay

SRG Action: Impact/Priority Score: 10    Percentile: 2
Human Subjects: 10-No human subjects involved
Animal Subjects: 10-No live vertebrate animals involved for competing appl.
Questions?